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10/533,618	02/06/2006	Martin Kintrup	30187/41217	1749

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,618	KINTRUP ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4,14-18 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-13 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and the 47 kd antigen in the reply filed on 10/9/2007 is acknowledged. The traversal is on the following ground(s):

1. That the common technical feature uniting the claims is not obvious in view of the cited art. Applicant argues that the rapid plasma reagin (RPR) test of West does not comprise immobilized cardiolipin. Applicant asserts that previous RPR test, like that of West, provide a VDRL antigen in liquid form.

2. That West teaches the RPR and RST tests separately, whereas the instant invention entails two reactions to be performed simultaneously.

3. That the restriction is improper because it does not meet the standards set forth in MPEP 803, because the examiner has not shown that there would be a serious search and examination burden imposed by searching all of the claimed inventions.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, despite applicant's assertions, the RPR test disclosed by West does contain immobilized cardiolipin. As evidenced by the RPR product information sheets from Omega Diagnostics (Omega Diagnostics Ltd., IMMUTREP RPR product sheet) and Becton, Dickinson, and Company (BD Macro-Vue RPR Card Tests) the RPR test comprises cardiolipin immobilized to carbon particles.

Regarding argument 2, as stated previously, while West does teach two separate tests, it would have been obvious (especially in view of Egglestone *et al*, as set forth below) to combine the cardiolipin antigen with the 47 kd antigen in a single test because West advises using a mixture of several test antigens to over come the sensitivity and specificity problems of the separate tests. Further, it was known in the art to use multiple antigens in immunochromatographic test strips, so one would have had every expectation of success in combining the two tests into one test strip.

Regarding argument 3, the standards set forth in MPEP 803 are not used to determine the propriety of restrictions in applications filed under 35 USC 371. The PCT rules are used to

determine whether there is unity of invention, and search burden is not a consideration in this determination.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-20 are pending. Claims 4, 14-18, and 20 are withdrawn as being drawn to non-elected inventions. Claims 1-3, 5-13, and 19 are currently under examination.

Information Disclosure Statement

The information disclosure statement filed on 4/20/2006 has been considered. An initialed copy is enclosed. References B1, B2, and C10 have not been considered because English language translations have not been provided.

Specification

The use of the trademark TWEEN has been noted in this application on page 11. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It is noted that the cited occurrence of improper use is only exemplary and applicant should review the specification to correct any other use of trademarks.

Claim Objections

Claims 1-3, 5-13, and 19 are objected to because of the following informalities: the claims are drawn, in part, to non-elected subject matter. Appropriate correction is required.

Claims 2 and 13 are objected to because of the following informalities: the claims contain the acronym VDRL. While acronyms are permissible shorthand in the claims, the first use should include the full recitation followed by the acronym in parentheses. Appropriate correction is required.

Claims 5, 10, and 13 are objected to because of the following informalities: the claims contain confusing Markush language. It is suggested that the claims be amended to read, "the antigens are selected from the group consisting of A, B, *and* C," or "the antigens are A, B, *or* C." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim is drawn to a carrier for diagnosis and/or follow-up of a Treponema infection comprising at least one immobilized cardiolipin and at lease one immobilized Treponema-specific antigen. Said carrier is characterized in that the VDRL antigen bands allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample.

The specification discloses an immunochromatographic test strip test where the VDRL antigen, as well as several other Treponema-specific antigens have been applied to nitrocellulose. In the examples, the test strip is contacted with patient serum, allowing any antibodies present in said serum to bind to the antigens on the test strip. Bound antibodies are then visualized by exposing the strip to anti-human IgG, IgM, or IgA antibodies conjugated with alkaline phosphatase. Colored substrate for alkaline phosphatase is added, and color can be seen where the antibody conjugate has bound to serum antibodies, which in turn, have bound to the antigen on the test strip. This type of sandwich immunoassay is standard in the art (see for example, Sambri *et al.*, Clin. Diag. Lab. Immunol., 8:534-539, 2001, IDS filed 4/20/2006).

In the described method, it is the addition of either anti-human IgG or IgM that allows differentiation between anti-VDRL IgG and IgM antibodies in the patient sample. Neither the specification, nor the art show any VDRL antigen that allows said differentiation. To do so, the VDRL would have to have immunoglobulin class-specific binding, and this has not been shown. Therefore, the specification does not provide written description for any antigen meeting the limitations of claim 13.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5-9, 11-13, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 5, 7-9, and 13 are rendered vague and indefinite by the use of the term "preferably." The term renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 6 recites the limitation "further controls" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is suggested that applicant amend the claim to read "carrier further comprises controls" rather than "carrier comprises further controls."

Claim 7 recites the limitation "one control" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 recites the limitation "one control" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 11 is rendered vague and indefinite by the phrase "the carrier is designed as a test strip." It is not clear what limitations are meant to be engendered by this phrase. The carrier either is a test strip or it is not.

Claim 12 is rendered vague and indefinite by the phrase "the carrier is designed as an immunoblot." It is not clear what limitations are meant to be engendered by this phrase. The carrier either is an immunoblot or it is not.

Claim 13 recites the limitation "the VDRL antigen bands" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 19 recites the limitation "the detection method" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-6, 10-11, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over West *et al.* (Sex. Transm. Inf., 78:282-285, Aug. 2002) in view of Egglestone *et al.* (Communicable Dis. Pub. Health, 3:15-162, 2000).

The instant claims are drawn to a carrier for diagnosis and/or follow-up of a Treponema infection, comprising a) at least one immobilized cardiolipin and b) at least one immobilized Treponema-specific antigen (claim 1); characterized in that the cardiolipin is present together with lecithin and cholesterol as VDRL antigen, said products being preferably present in a mass ratio of cardiolipin:lecithin:cholesterol of 0.1-4.0:1-5.0:1-10 (claim 2); characterized in that the antigens are selected from Treponema pallidum-specific antigen, preferably the 15 kD, 17 kD, 44.5 kD and 47 kD antigen (claim 5); characterized in that the carrier comprises further controls (claim 6); characterized in that the carrier is selected from nitrocellulose, PVDF (polyvinylidene difluoride), nylon, cellulose acetate, polystyrene (claim 10); characterized in that the carrier is designed as a test strip for use in immunodiagnostics (claim 11); characterized in that the VDRL antigen bands applied to the carrier allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample, preferably selected from blood, serum, plasma, liquor or synovial fluid (claim 13); and to a test kit for the diagnosis of a Treponema infection and/or the follow-up of a Treponema infection, comprising a carrier

according to claim 1 and further reagents as well as an instruction manual for carrying out the detection method (claim 19).

West *et al.* disclose two tests for the detection of syphilis, the RPR test and RST (see abstract). As evidenced by the RPR product information sheets from Omega Diagnostics (Omega Diagnostics Ltd., IMMUTREP RPR product sheet) and Becton, Dickinson, and Company (BD Macro-Vue RPR Card Tests), the RPR test is an agglutination test where VDRL antigen (cardiolipin, lecithin, and cholesterol) is immobilized on carbon particles (a carrier). The RST is a immunochromatographic strip test that contains the 47 kD *Treponema pallidum* antigen immobilized in a line on a test strip (carrier), as well as a control line (see page 282, column 1, paragraph 1 and page 282, column 2, paragraph 3).

West *et al.* differs from the instant invention in that the VDRL antigen and the 47 kD antigen are not immobilized on a single carrier, the control is not disclosed as a serum or cut-off control, and the carrier material is not disclosed as nitrocellulose, PVDF, nylone, cellulose, acetate, or polystyrene. The test is also not specifically disclosed as containing instructions for use.

Egglestone *et al.* disclose recommendations for serological diagnosis of syphilis. Egglestone *et al.* disclose using a combination of a quantitative non-treponemal test (such as the VDRL and RPR tests, which use cardiolipin antigens) with a specific treponemal immunoassay (see page 159, column 2). Egglestone *et al.* states that combining the non-treponemal test with an assay for specific anti-treponemal IgM helps to assess the stage of infection and provide a baseline for monitoring treatment (see page 160, column 2, paragraph 3). Egglestone *et al.* specifically recommend combining a treponemal immunoassay (for IgM, IgG, or both) with a non-treponemal test (see page 162, recommendation 3).

Therefore, it would have been obvious to one of skill in the art, at the time of invention, to use the VDRL antigen (as disclosed by West *et al.* and Egglestone *et al.*) on the immunochromatographic test strip disclosed by West *et al.*, thus combining the two tests into one, for ease of use and because Egglestone *et al.* recommends using both tests in the diagnosis of syphilis. It would also have been obvious to use nitrocellulose, PVDF, nylone, cellulose,

acetate, or polystyrene as the strip material because immunochromatographic test strips are common in the art and these materials are the standard materials in such strips.

One would have had a reasonable expectation of success because immunochromatographic tests performed using test strips are commonly used in the art with numerous different antigens. Further, immunoassays using VDRL antigen and the 47 kD treponemal antigen have been shown to be successful by West *et al.*

With regard to claim 19, according to MPEP 2112.01, Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004).

Claims 1-3, 5-12, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zarakolu *et al.* (J. Clin. Microbiol., 40:3064-6065, Aug. 2002) in view of Sambri *et al.* (Clin. Diag. Lab. Immunol., 8:534-539, 2001).

The instant claims are drawn to a carrier for diagnosis and/or follow-up of a Treponema infection, comprising a) at least one immobilized cardiolipin and b) at least one immobilized Treponema-specific antigen (claim 1); characterized in that the cardiolipin is present together with lecithin and cholesterol as VDRL antigen, said products being preferably present in a mass ratio of cardiolipin:lecithin:cholesterol of 0.1-4.0:1-5.0:1-10 (claim 2); characterized in that the cardiolipin is present in at least two, preferably at least three, particularly preferably at least four different concentrations at different positions of the carrier (claim 3); characterized in that the antigens are selected from Treponema pallidum-specific antigen, preferably the 15 kD, 17 kD, 44.5 kD and 47 kD antigen (claim 5); characterized in that the carrier comprises further controls (claim 6); characterized in that one control is a serum control, preferably protein A (claim 7); characterized in that one control is a cut-off control, preferably comprising purified human immunoglobulin (claim 8); characterized in that it comprises a serum control which preferably comprises protein A and a cut-off control which preferably comprises human immunoglobulin (claim 9); characterized in that the carrier is selected from nitrocellulose, PVDF (polyvinylidene difluoride), nylon, cellulose acetate, polystyrene (claim 10); characterized in that the carrier is

designed as a test strip for use in immunodiagnostics (claim 11); characterized in that the carrier is designed as an immunoblot (claim 12); characterized in that the VDRL antigen bands applied to the carrier allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample, preferably selected from blood, serum, plasma, liquor or synovial fluid (claim 13); and to a test kit for the diagnosis of a Treponema infection and/or the follow-up of a Treponema infection, comprising a carrier according to claim 1 and further reagents as well as an instruction manual for carrying out the detection method (claim 19).

Zarakolu *et al.* disclose an immunochromatographic test strip where the 47 kD treponemal antigen has been immobilized in a thin line on nitrocellulose strips. The strips also contain a line of anti-human IgG to serve as a control (see page 3064, column 2, paragraph 2). The line of anti-human IgG would serve as both a serum control and as a cut-off control, as it would indicate the presence of serum and immunoglobulins. Zarakolu *et al.* also disclose the RPR test and disclose that syphilis testing is usually a two step procedure where non-treponemal tests (such as RPR) are used in combination with specific tests for treponemal antigens (see page 3064, column 1, paragraph 1).

Zarakolu *et al.* differ from the instant claims in that the VDRL antigen is not disclosed on the same carrier as the 47 kD antigen, the VDRL antigen is not present in at least two concentrations at different positions of the carrier, the test is not disclosed as having been designed as an immunoblot, and the test is not disclosed as containing instructions for use.

Sambri *et al.* disclose a Western blot test where test strips were created with different antigens in different positions on nitrocellulose strips (see page 535, column 2, paragraphs 2-3).

Therefore, it would have been obvious to one of skill in the art, at the time of invention, to use the VDRL antigen on the immunochromatographic test strip disclosed by Zarakolu *et al.*, thus combining the two tests into one, for ease of use and because both tests are generally used in the diagnosis of syphilis. Additionally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it is obvious to substitute one known component for another where one of ordinary skill in the art could have substituted one known element for another, and the results would have been predictable. Thus, it would have been obvious to use multiple concentrations of VDRL antigen in different positions on the

test strip of either Zarakolu *et al.* or Sambri *et al.* instead of multiple treponemal antigens because one would achieve predictable results.

One would have had a reasonable expectation of success because immunochromatographic tests performed using test strips are commonly used in the art with numerous different antigens (as evidenced by Sambri *et al.*). Further, immunoassays using VDRL antigen and the 47 kD treponemal antigen have been shown to be successful by Zarakolu *et al.*

With regard to claim 19, according to MPEP 2112.01, Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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